

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-986

MICROBIOLOGY REVIEW(S)

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGISTS REVIEW OF NDA 20-986
4 February 1999

A. 1. NDA 20-986 BI

APPLICANT: Novo Nordisk Pharmaceuticals, Inc.
Suite 200
100 Overlook Center
Princeton, NJ 08540-7810

2. PRODUCT NAME: Insulin Aspart (Insulin X-14) Injection (recombinant DNA origin)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is a sterile injectable preparation for subcutaneous injection.

4. METHODS OF STERILIZATION:
The product is _____

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The drug product is indicated in the treatment of diabetes mellitus.

B. 1. DATE OF INITIAL SUBMISSION: 16 September 1998

2. DATE OF AMENDMENT: 29 January 1999 (Subject of this Review)

3. RELATED DOCUMENTS: IND _____; NDA 19-938; DMF _____
DMF _____; DMF _____

4. ASSIGNED FOR REVIEW: 30 September 1998

C. REMARKS: The product will be manufactured by:

Novo Nordisk A/S
Novo Alle
DK-2880 Bagsvaerd
Denmark

The product is to be packaged in the following presentations:

10 mL vial

PenFill® 3 mL cartridge

Prefilled® 3 mL syringe

It is the applicant's intent to market only the 10mL vial, Penfill® 3mL cartridge, and Prefilled® 3mL syringe at the present time. Should Novo Nordisk decide the other presentations, labeling will be submitted to the Agency for review.

D. CONCLUSIONS: The application is recommended for approval on the basis of sterility assurance.

[Signature]
Paul Stinavage, Ph.D. 4 February 1999
[Signature] 2/8/99

cc: Original NDA 20-986
HFD-510/J. Rhee/Div. File
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 4 February 1999
R/D initialed by P. Cooney

APPEARS THIS WAY
ON ORIGINAL

2/3/99

TO (Division Office): Paul Stinavage, Ph.D., HFD-160

FROM: HFD-510 (Division of Metabolic and Endocrine Drug Products) Julie Rhee

E bruary 3, 1999	IND NO.:	NDA NO.: 20-986	TYPE OF DOCUMENT : Microbiology response	DATE OF DOCUMENT: January 29, 1999
NAME OF DRUG: Insulin Aspart (insulin X-14 [rDNA])		PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE March 15, 1999

NAME OF FIRM: Novo Nordisk

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> SAFETY/EFFICACY | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | | |

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- | | |
|--|---|
| <input type="checkbox"/> TYPE A OR B NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER: |

P: /S/ /S/ 2/3/99

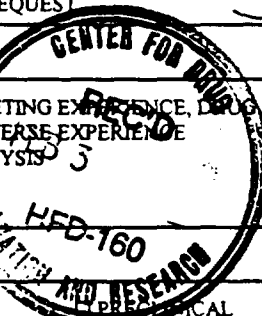
III. BIOPHARMACEUTICS

- | | |
|--|---|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE IV STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG EXPERIENCE

- | | |
|--|--|
| <input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Paul, this is Novo's response to your earlier requests. For your information, a copy of the fax that was sent to Novo is attached. Thank you.

cc: Original NDA 20-986
HFD-510/Div. Files

SIGNATURE OF REQUESTER: <i>/S/</i>	METHOD OF DELIVERY (Check one): <input type="checkbox"/> MAIL <input checked="" type="checkbox"/> HAND
SIGNATURE OF RECEIVER: <i>/S/ 2-3-99</i>	SIGNATURE OF DELIVERER: <i>/S/ 2-3-99</i>

JAN - 4 1999

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGISTS REVIEW OF NDA 20-986
4 January 1999

A. 1. NDA 20-986

APPLICANT: Novo Nordisk Pharmaceuticals, Inc.
Suite 200
100 Overlook Center
Princeton, NJ 08540-7810

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3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
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4. METHODS OF STERILIZATION:
The product is _____

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The drug product is indicated in the treatment of diabetes mellitus.

B. 1. DATE OF INITIAL SUBMISSION: 16 September 1998

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: IND _____ ; NDA 19-938; DMF _____
DMF _____ DMF _____

4. ASSIGNED FOR REVIEW: 30 September 1998

C. REMARKS: The product will be manufactured by:

Novo Nordisk A/S
Novo Alle
DK-2880 Bagsvaerd
Denmark

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D. CONCLUSIONS: The application is approvable pending resolution of microbiology concerns.

TS/ 4 January 1999
TS/ 1/4/99
Paul Stinavage, Ph.D.

cc: Original NDA 20-986
HFD-510/J. Rhee/Div. File
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 4 January 1999
R/D initialed by P. Cooney

**APPEARS THIS WAY
ON ORIGINAL**

TO (Division/Office):

HFD-805 Microbiology Peter Cooney

FROM:

HFD-510 (Division of Metabolism & Drug Products)

9/23/98

DATE

September 23, 1998

IND NO.

NDA NO.

20-986

TYPE OF DOCUMENT

DATE OF DOCUMENT

Sept 16, 1998

NAME OF DRUG

Insulin Aspart X-14

PRIORITY CONSIDERATION

STANDARD

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE

July 30, 1999

NAME OF FIRM:

Novo Nordisk Pharmaceuticals

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY

- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT

- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER (SPECIFY BELOW): Micro

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

- ☐ TYPE A OR B NDA REVIEW
- ☐ END OF PHASE II MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):

STATISTICAL APPLICATION BRANCH

- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILITY STUDIES
- ☐ PHASE IV STUDIES

- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

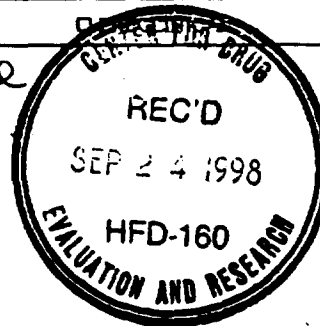
V. SCIENTIFIC INVESTIGATIONS

CLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

(Project Manager 7-6424)

TO: P. Strnava
1/S/
9/30/98



SIGNATURE OF REQUESTER

1/S/ for Julie Rhee 9/23/98

METHOD OF DELIVERY (Check one)

☒ MAIL

☐ HAND

NATURE OF RECEIVER

1/S/

SIGNATURE OF DELIVERER